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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,388	10/07/2003	John H. Kenten	IGN-2005US03	7445

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/681,388	KENTEN ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 10/18/2005, including arguments/remarks and amendments to the claims and specification, was received on 4/21/2006 and has been made of record.

2. The text of those sections of Title 35, U.S.C. not included in this action can be found cited in full, in the previous office action mailed on 10/18/2005

3. Claim 86 is currently pending and is the subject of this office action.

Specification

1. Objection to the title of the application as not being descriptive of the claimed invention, as set forth on p. 2 of the office action mailed on 10/18/2005, is *withdrawn* in response to the Applicants' amending the title to "Method of identification using ubiquitin-fusion proteins."

2. Objection to the specification for being incomplete in regards to omitting bibliographic data from the 1st paragraph of the specification, as set forth on p. 2 of the office action mailed on 10/18/2005, is *withdrawn* in response to Applicants' amendment to the 1st paragraph of the specification to reflect the current bibliographic data.

3. Objection to the specification for missing sequence identifiers, as set forth on p. 2 of the office action mailed on 10/18/2005, is *withdrawn* in response to Applicants' amendment to the specification to including the proper sequence identifiers.

Claim Objections

1. Objection to claim 86 for reciting a "fusion protein *of* selected from the group.....", as set forth on p. 3 of the office action mailed on 10/18/2005, is *withdrawn* in response to the amendments to the claim to remove the "of" between "protein" and "selected".

2. Amended claim 86 is objected to because the claim reads on a ubiquitin fusion protein comprising "ubiquitin fused to two *of* more non-contingous.....". The Examiner suggests amending the claim to read "two or more.....".

3. Amended claim 86 is objected to for the following minor spelling error: part (a, *iii*) recites ".....at fusion sites selected form the groups consisting of.....". The Examiner has interpreted this to mean ".....at fusion sites selected *from* the groups....."

Claim Rejections - 35 USC § 101

Rejection of claim 86 under 35 USC § 101, for lacking a specific, substantial, or credible utility, as set forth on p. 3 of the prior Office Action mailed on 10/18/2005, is *withdrawn* in response to the Applicants arguments that the amendments to the claim better discern the Applicant's invention, and in this light the utility rejection is moot.

Claim Rejections - 35 USC § 112, first paragraph, enablement

Rejections withdrawn

1. Claim 86 was rejected under 35 USC § 101, for lacking a specific, substantial, or credible utility. As set forth on p. 4 of the prior Office Action mailed on 10/18/2005, the claim was also rejected under 35 USC § 112, first paragraph. Specifically, because the claimed invention was found to not be supported by either a specific asserted utility or a well-established utility for the reasons set forth on p. 3 of the office action mailed on 10/18/2005, one skilled in the art would not know how to use the claimed invention. However, because the rejection under 35 USC § 101 has been withdrawn, this accompanying rejection under 35 USC § 112, first paragraph, is also *withdrawn*.

2. Rejection of claim 86 under 35 USC § 112, first paragraph, regarding lack of enablement for a method using an antigen comprising ubiquitin fused to any protein antigen, as set forth on p. 4 of the office action mailed on 10/18/2005, is *withdrawn* in response to the Applicant's arguments that the specification provides exemplanary embodiments of the claimed invention, and the amendments to the claim to further limit the nature of the claimed ubiquitin fusion protein antigen used in the method of the instant invention.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejection of claim 86 under 35 USC § 112, first paragraph, regarding lack of written description for ubiquitin fusion proteins comprising ubiquitin fused to one or more antigenic epitopes, as set forth on p. 5-6 of the office action mailed on 10/18/2005, is *withdrawn* in response Applicant's arguments that antigenicity is an identifying characteristic, and the amendments to the claims to further limit the nature of the fusion protein.

Claim Rejections - 35 USC § 112, second paragraph

Rejections withdrawn

1. Rejection of claim 86 under 35 USC § 112, second paragraph, as being indefinite for depending from cancelled claims, as set forth on p. 6 of the office action mailed on 10/18/2005, is *withdrawn* in response Applicant's amendments to the claim to remove dependency from the cancelled claims.

Rejections necessitated by amendment

2. Claim 86 recites the limitation "....fused to ubiquitin at the N-terminus of *the* heat shock protein" (a, iv). There is insufficient antecedent basis for this limitation in the claim because the term heat shock protein does not appear elsewhere in the claim.

3. Claim 86 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Part a (*iii*) recites "a ubiquitin fusion protein comprising ubiquitin fused to a single

epitope-containing segment", and further recites ""the epitope-containing *segments* being fused to the ubiquitin at fusion sites selected form the *groups* consisting of the N-terminus and an internal fusion site". The meaning of the phrase "epitope-containing segments" is unclear because the part a (*iii*) is drawn to a fusion protein fused to a single epitope-containing segment, and thus the wording of the claim referring to more than one epitope-containing segments is unclear.

Additionally, part a (*iii*) also refers to "fusion sites selected form the groups", while the claim only contains a single group from which to select fusion sites, and thus the meaning of the wording referring to more than one group is unclear.

4. Claim 86 (a, *iv*) recites the limitation "wherein one or more epitopes are recognized by the antibody to be detected". There is insufficient antecedent basis for this limitation in the claim because it is not clear if the antibody of the claimed method is to detect one or more epitopes from parts *i* - *iv*, or just part *iv*.

Claim Rejections - 35 USC § 102

1. Claim 86 *remains rejected* under 35 USC § 102(b) as being anticipated by Vannier *et al*, as set forth on p. 6-7 of the prior Office Action mailed on 10/18/2005. Vannier *et al* teaches a method of identifying antibodies from experimental samples using an ubiquitin-follicle stimulating hormone receptor (FSHR) fusion protein. In the response received on 4/21/2006, the Applicant's argue that Vannier *et al* does not anticipated the claims as currently amended because Vannier *et al* does not teach a fusion protein wherein ubiquitin is either (i) fused to a single epitope-containing segment, the epitope-containing segment comprising two or more identical epitopes, (ii), fused to two or more non-contiguous epitope-containing segments, each epitope-containing segments comprising one or more identical or non-identical epitopes, (iii), fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segments being fused to the ubiquitin at fusion sites selected from the groups consisting of the N-terminus and an internal fusion site, or (iv) fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, the

epitope-containing segment being fused to ubiquitin at the N-terminus of the heat shock protein, wherein one or more epitopes are recognized by the antibody to be detected.

This argument has been fully considered and is not found persuasive. It is noted that the claim recite fusion proteins "comprising" various epitopes or epitope-containing segments. The use of the phrase "comprising" is open-ended, and thus the limitations of the claim can be met by any protein that contains an epitope-containing fragment, or two or more epitope-containg fragments. While Vannier *et al* does not explicitly teach an uniquitin fusion protein meeting the limitations recited in the claim, it would be expected that the ubiquitin-FSHR protein taught by Vannier *et al* would inherently meet at least one of these limitations. The specification, on p. 6, lines 17-19, defines epitopes as "recombinant immunologically active heterologous antigens (referred to herein as epitopes)". The ubiquitin-FSHR protein taught by Vannier *et al* is a recombinant protein, and FSHR would be expected to be comprised of two or more epitope-containing segments (as defined as immunologically active antigens), with each epitope-containing segment comprising one or more identical or non-identical epitopes. Alternatively, the fusion protein taught by Vannier *et al* could also be considered to be a fusion protein *comprising* a single epitope (FSHR – which in this case is a recombinant immunologically active heterologous antigen), with said single epitope further comprising two or more identical or non-identical epitopes.

The office does not have the facilities for determining the exact nature of the epitopes that comprise FSHR. Therefore the burden is on the applicant to show a novel and unobvious difference between the claimed ubiquitin fusion protein and that of Vannier *et al*. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). In other words, the burden is on the Applicant to show that the ubiquitin-FSHR protein of Vannier *et al* is not a fusion protein wherein ubiquitin is either (i) fused to a single epitope-containing segment, the epitope-containing segment comprising two or more identical epitopes, (ii), fused to two or more non-contiguous epitope-containing segments, each epitope-containing segments comprising one or more identical or non-identical epitopes, (iii), fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segments being fused to the ubiquitin at fusion sites selected from the groups consisting of the N-terminus and an internal fusion site, or (iv) fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, the

epitope-containing segment being fused to ubiquitin at the N-terminus of the heat shock protein, wherein one or more epitopes are recognized by the antibody to be detected.

2. Claim 86 *remains rejected* under 35 USC § 102(b) as being anticipated by Loosfelt *et al*, as set forth on p. 7 of the prior Office Action mailed on 10/18/2005. Loosfelt *et al* teaches a method of identifying thyrotropin receptor (TSHR)-specific antibodies from experimental samples using an ubiquitin-TSHR fusion protein. In the response received on 4/21/2006, the Applicant's argue that Loosfelt *et al* does not anticipated the claims as currently amended because Loosfelt *et al* does not teach a fusion protein wherein ubiquitin is either (i) fused to a single epitope-containing segment, the epitope-containing segment comprising two or more identical epitopes, (ii), fused to two or more non-contiguous epitope-containing segments, each epitope-containing segments comprising one or more identical or non-identical epitopes, (iii), fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segments being fused to the ubiquitin at fusion sites selected from the groups consisting of the N-terminus and an internal fusion site, or (iv) fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, the epitope-containing segment being fused to ubiquitin at the N-terminus of the heat shock protein, wherein one or more epitopes are recognized by the antibody to be detected.

This argument has been fully considered and is not found persuasive. It is noted that the claim recite fusion proteins "comprising" various epitopes or epitope-containing segments. The use of the phrase "comprising" is open-ended, and thus the limitations of the claim can be met by any protein that contains an epitope-containing fragment, or two or more epitope-containg fragments. While Loosfelt *et al* does not explicitly teach an uniquitin fusion protein meeting the limitations recited in the claim, it would be expected that the ubiquitin-TSHR protein taught by Loosfelt *et al* would inherently meet at least one of these limitations. The specification, on p. 6, lines 17-19, defines epitopes as "recombinant immunologically active heterologous antigens (referred to herein as epitopes)". The ubiquitin-TSHR protein taught by Loosfelt *et al* is a recombinant protein, and TSHR would be expected to be comprised of two or more epitope-containing segments (as defined as immunologically active antigens), with each epitope-containing segment comprising one or more identical or non-identical epitopes. Alternatively, the fusion protein taught by Loosfelt *et al* could also be considered to be a fusion protein *comprising* a single epitope (TSHR – which in this case is a recombinant

immunologically active heterologous antigen), with said single epitope further comprising two or more identical or non-identical epitopes.

The office does not have the facilities for determining the exact nature of the epitopes that comprise TSHR. Therefore the burden is on the applicant to show a novel and unobvious difference between the claimed ubiquitin fusion protein and that of Vannier *et al.* See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). In other words, the burden is on the Applicant to show that the ubiquitin-TSHR protein of Loosfelt *et al* is not a fusion protein wherein ubiquitin is either (i) fused to a single epitope-containing segment, the epitope-containing segment comprising two or more identical epitopes, (ii), fused to two or more non-contiguous epitope-containing segments, each epitope-containing segments comprising one or more identical or non-identical epitopes, (iii), fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segments being fused to the ubiquitin at fusion sites selected from the groups consisting of the N-terminus and an internal fusion site, or (iv) fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, the epitope-containing segment being fused to ubiquitin at the N-terminus of the heat shock protein, wherein one or more epitopes are recognized by the antibody to be detected.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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